Additionally, ACT is further limited due to the fact that once accumulated at the tumor site, the T cell response is repressed by various means. The tumor microenvironment may prevent efficient infiltration by repressor cells, secreted soluble factors from the tumor or stroma cells and by nutrient deprivation. Moreover, T cells express multiple immune repressive receptors which, upon activation, repress the T cell response, including e.g. cytotoxic T lymphocyte-associated antigen-4 (CTLA-4) and programmed cell death-1 (PD-1). Future clinical models need to counteract and overcome T cell repression while retaining tumor specificity and cytotoxicity.

Accordingly, the targeted tumor therapy, particularly the adoptive T cell therapy is still in need of more differentiated tools in order to suffice the needs of the cancer patients. Thus, there is still a need to provide new means having the potential to improve safety and efficacy of ACT and overcome the above disadvantages.

SUMMARY

The present disclosure generally relates to new antigen binding receptor formats capable of specific binding to distinct targets, i.e. a tumor associated antigen (TAA) and T cells expressing these antigen binding receptors. The antigen binding receptors of the disclosure lead to strong and selective activation of T cells upon binding of one or more antigen binding receptors to a target cell, i.e. to a tumor cell.

The disclosure relates to an antigen binding receptor comprising an anchoring transmembrane domain and an extracellular domain comprising an antigen binding moiety, wherein the antigen binding moiety is a Fab, crossFab or a scFab fragment.

In one aspect, the disclosure relates to an antigen binding receptor comprising an anchoring transmembrane domain and an extracellular domain comprising an antigen binding moiety, wherein the antigen binding moiety is a Fab or crossFab, wherein the antigen binding receptor comprises, at least one stimulatory signaling domain and at least one co-stimulatory signaling domain, wherein the at least one stimulatory signaling domain is the intracellular domain of CD3z, wherein the at least one co-stimulatory signaling domain is the CD28 intracellular domain.

In one example, the anchoring transmembrane domain is a transmembrane domain selected from the group consisting of the CD8, the CD3z, the FCGR3A, the NKG2D, the CD27, the CD28, the CD137, the OX40, the ICOS, the DAP10 or the DAP12 transmembrane domain or a fragment thereof.

In one example, the anchoring transmembrane domain is the CD28 transmembrane domain or a fragment thereof, in particular wherein the anchoring transmembrane domain comprises the amino acid sequence of SEQ ID NO:14.

In one example, the antigen binding receptor further comprises at least one stimulatory signaling domain and/or at least one co-stimulatory signaling domain.

In one example, the at least one stimulatory signaling domain is individually selected from the group consisting of the intracellular domain of CD3z, of FCGR3A and of NKG2D, or fragments thereof.

In one example, the at least one stimulatory signaling domain is the intracellular domain of CD3z or a fragment thereof, in particular wherein the at least one stimulatory signaling domain comprises the amino acid sequence of SEQ ID NO:16.

In one example, the at least one co-stimulatory signaling domain is individually selected from the group consisting of the intracellular domain of CD27, of CD28, of CD137, of OX40, of ICOS, of DAP10 and of DAP12, or fragments thereof.

In one example, the at least one co-stimulatory signaling domain is the CD28 intracellular domain or a fragment thereof, in particular, wherein the at least one co-stimulatory signaling domain comprises the amino acid sequence of SEQ ID NO:15.

In one example, the antigen binding receptor comprises one stimulatory signaling domain comprising the intracellular domain of CD3z, or a fragment thereof, and wherein the antigen binding receptor comprises one co-stimulatory signaling domain comprising the intracellular domain of CD28, or a fragment thereof.

In one example, the stimulatory signaling domain comprises the amino acid sequence of SEQ ID NO:16 and the co-stimulatory signaling domain comprises the amino acid sequence of SEQ ID NO:15.

In one example, the extracellular domain is connected to the anchoring transmembrane domain, optionally through a peptide linker.

In one example, the peptide linker comprises the amino acid sequence GGGGS (SEQ ID NO:20).

In one example, the anchoring transmembrane domain is connected to a co-signaling domain or to a signaling domain, optionally through a peptide linker.

In one example, the signaling and/or co-signaling domains are connected, optionally through at least one peptide linker.

In one example, the antigen binding moiety comprises a heavy chain constant (CH) domain and a light chain constant domain (CL), wherein the CH domain or the CL domain is connected at the C-terminus to the N-terminus of the anchoring transmembrane domain, optionally through a peptide linker.

In one example, the antigen binding receptor comprises one co-signaling domain, wherein the co-signaling domain is connected at the N-terminus to the C-terminus of the anchoring transmembrane domain.

In one example, the antigen binding receptor additionally comprises one stimulatory signaling domain, wherein the stimulatory signaling domain is connected at the N-terminus to the C-terminus of the co-stimulatory signaling domain.

In one example, the antigen binding moiety is capable of specific binding to an antigen selected from the group consisting of FAP, CEA, p95, BCMA, EpCAM, MSLN, MCSP, HER-1, HER-2, HER-3, CD19, CD20, CD22, CD33, CD38, CD52Flt3, FOLR1, Trop-2, CA-12-5, HLA-DR, MUC-1 (mucin), A33-antigen, PSMA, PSCA, transferrin-receptor, TNC (tenascin), CA-IX and PDL1, or to a peptide bound to a molecule of the human major histocompatibility complex (MHC).

In one example, the antigen binding moiety is capable of specific binding to an antigen selected from the group consisting of fibroblast activation protein (FAP), carcinoembryonic antigen (CEA), mesothelin (MSLN), CD20, folate receptor 1 (FOLR1), tenascin (TNC) and programmed death-ligand 1(PDL1).

In one example, the antigen binding moiety is a capable of specific binding to CD20, wherein the antigen binding moiety comprises:

(i) a heavy chain variable region (VH) comprising

(a) the heavy chain complementarity-determining region (CDR H) 1 amino acid sequence YSWIN (SEQ ID NO:1);

(b) the CDR H2 amino acid sequence RIFPGDGDTDYNGKFKG (SEQ ID NO:2); and

(c) the CDR H3 amino acid sequence NVFDGYWLVY (SEQ ID NO:3); and

(ii) a light chain variable region (VL) comprising

(d) the light chain complementary-determining region (CDR L) 1 amino acid sequence RSSKSLLHSNGITYLY (SEQ ID NO:4);

(e) the CDR L2 amino acid sequence QMSNLVS (SEQ ID NO:5); and

(f) the CDR L3 amino acid sequence AQNLELPYT (SEQ ID NO:6).

In one example, the antigen binding moiety is capable of specific binding to CD20, wherein the antigen binding moiety comprises a heavy chain variable region (VH) comprising an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid of SEQ ID NO:12, and a light chain variable region (VL) comprising an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO:10.

In one example, the antigen binding moiety comprises the heavy chain variable region (VH) of SEQ ID NO:12 and the light chain variable region (VL) of SEQ ID NO:10.

In one example, the antigen binding moiety is a Fab fragment capable of specific binding to CD20, wherein the antigen binding receptor comprises

a) a first polypeptide that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:7 and SEQ ID NO:50; and

b) a second polypeptide that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:9 and SEQ ID NO:8.

In one example, the antigen binding moiety is a crossFab fragment capable of specific binding to CD20, wherein the antigen binding receptor comprises

a) a first polypeptide that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:36 and SEQ ID NO:41; and

b) a second polypeptide that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:38 and SEQ ID NO:43.

In one example, the antigen binding moiety is a scFab fragment capable of specific binding to CD20, wherein the antigen binding receptor comprises a polypeptide that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO:51.

In one example, the antigen binding moiety is a capable of specific binding to PDL1, wherein the antigen binding moiety comprises:

(i) a heavy chain variable region (VH) comprising

(a) the heavy chain complementarity-determining region (CDR H) 1 amino acid sequence DSWIH (SEQ ID NO:68);

(b) the CDR H2 amino acid sequence WISPYGGSTYYADSVKG (SEQ ID NO:69); and

(c) the CDR H3 amino acid sequence RHWPGGFDY (SEQ ID NO:70); and

(ii) a light chain variable region (VL) comprising

(d) the light chain complementary-determining region (CDR L) 1 amino acid sequence RASQDVSTAVA (SEQ ID NO:71);

(e) the CDR L2 amino acid sequence SASFLYS (SEQ ID NO:72); and

(f) the CDR L3 amino acid sequence QQYLYHPAT (SEQ ID NO:73).

In one example, the antigen binding moiety is capable of specific binding to PDL1, wherein the antigen binding moiety comprises a heavy chain variable region (VH) comprising an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to

the amino acid of SEQ ID NO:78, and a light chain variable region (VL) comprising an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO:77.

In one example, the antigen binding moiety comprises the heavy chain variable region (VH) of SEQ ID NO:78 and the light chain variable region (VL) of SEQ ID NO:77.

In one example, the antigen binding moiety is a Fab fragment capable of specific binding to PDL1, wherein the antigen binding receptor comprises

a) a first polypeptide that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:74 and SEQ ID NO:85; and

b) a second polypeptide that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:76 and SEQ ID NO:75.

In one example, the antigen binding moiety is a crossFab fragment capable of specific binding to PDL1, wherein the antigen binding receptor comprises

a) a first polypeptide that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:79 and SEQ ID NO:82; and

b) a second polypeptide that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:81 and SEQ ID NO:84.

In one example, the antigen binding moiety is a scFab fragment capable of specific binding to PDL1, wherein the antigen binding receptor comprises a polypeptide that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO:86.

In one example, the antigen binding moiety is a capable of specific binding to CEA, wherein the antigen binding moiety comprises:

(i) a heavy chain variable region (VH) comprising

(a) the heavy chain complementarity-determining region (CDR H) 1 amino acid sequence EFGMN (SEQ ID NO:138);

(b) the CDR H2 amino acid sequence WINTKTGEATYVEEFKG (SEQ ID NO:139); and

(c) the CDR H3 amino acid sequence WDFAYYVEAMDY (SEQ ID NO:140); and

(ii) a light chain variable region (VL) comprising

(d) the light chain complementary-determining region (CDR L) 1 amino acid sequence KASAAVGTYVA (SEQ ID NO:141);

(e) the CDR L2 amino acid sequence SASYRKR (SEQ ID NO:142); and

(f) the CDR L3 amino acid sequence HQYYTYPLFT (SEQ ID NO:143).

In one example, the antigen binding moiety is a capable of specific binding to CEA, wherein the antigen binding moiety comprises:

(i) a heavy chain variable region (VH) comprising

(a) the heavy chain complementarity-determining region (CDR H) 1 amino acid sequence DTYMH (SEQ ID NO:148);

(b) the CDR H2 amino acid sequence RIDPANGNSKYVPKFQG (SEQ ID NO:149); and

(c) the CDR H3 amino acid sequence FGYYVSDYAMAY (SEQ ID NO:150); and

(ii) a light chain variable region (VL) comprising

(d) the light chain complementary-determining region (CDR L) 1 amino acid sequence RAGESVDIFGVGFLH (SEQ ID NO:151);

(e) the CDR L2 amino acid sequence RASNRAT (SEQ ID NO:152); and

(f) the CDR L3 amino acid sequence QQTNEDPYT (SEQ ID NO:153).

In another aspect, provided is an isolated polynucleotide encoding the antigen binding receptor as described herein.

Provided is a composition encoding the antigen binding receptor as described herein, comprising a first isolated polynucleotide encoding a first polypeptide, and a second isolated polynucleotide encoding a second polypeptide.

Provided is a polypeptide encoded by the polynucleotide as described herein or by the composition as described herein.

Provided is a vector, particularly an expression vector, comprising the polynucleotide as described herein or the composition as described herein.

In another aspect, provided is a vector comprising the isolated polynucleotide as described herein.

Provided is a transduced T cell comprising the polynucleotide as described herein, the composition as described herein or the vector as described herein.

In another aspect, provided is a transduced T cell capable of expressing at least one of the antigen binding receptors as described herein.

In one example, provided is the transduced T cell as described herein, wherein the cell comprises

(i) not more than one antigen binding receptor comprising a Fab (VH-CH-ATD) antigen binding domain;

(ii) not more than one antigen binding receptor comprising a Fab (VL-CL-ATD) antigen binding domain;
(iii) not more than one antigen binding receptor comprising a crossFab (VL-CH-ATD) antigen binding domain; and
(iv) not more one antigen binding receptor comprising a crossFab (VH-CL-ATD) antigen binding domain.

In one example, provided is the transduced T cell as described herein, wherein the cell comprises a first antigen binding receptor as described herein, wherein a first antigen binding receptor comprises a Fab antigen binding moiety, and wherein the cell comprises a second antigen binding receptor as described herein, wherein the second antigen binding receptor comprises a crossFab antigen binding moiety.

In one example, provided is the transduced T cell as described herein, wherein the cell comprises a first antigen binding receptor as described, wherein the first antigen binding receptor comprises a Fab (VH-CH-ATD) antigen binding moiety, and wherein the cell comprises a second antigen binding receptor as described herein, wherein the second antigen binding receptor comprises a Fab (VL-CL-ATD) antigen binding moiety.

In one example, provided is the transduced T cell as described herein, wherein the cell comprises a first antigen binding receptor as described herein, wherein the first antigen binding receptor comprises a crossFab (VL-CH-ATD) antigen binding moiety, and wherein the cell comprises a second antigen binding receptor as described herein, wherein the second antigen binding receptor comprises a crossFab (VH-CL-ATD) antigen binding moiety.

In one example, provided is the transduced T cell as described herein, wherein the cell comprises a first antigen binding receptor as described herein, wherein a first antigen binding receptor comprises a scFab antigen binding moiety, and wherein the cell comprises a second antigen binding receptor as described herein, wherein the second antigen binding receptor comprises an scFv, a Fab or crossFab antigen binding moiety.

In one example, provided is the transduced T cell as described herein, wherein the cell comprises a first antigen binding receptor capable of specific binding to an antigen selected from the group consisting of FAP, CEA, p95, BCMA, EpCAM, MSLN, MCSP, HER-1, HER-2, HER-3, CD19, CD20, CD22, CD33, CD38, CD52Flt3, FOLR1, Trop-2, CA-12-5, HLA-DR, MUC-1 (mucin), A33-antigen, PSMA, PSCA, transferrin-receptor, TNC (tenascin), CA-IX and PDL1, or to a peptide bound to a molecule of the human major histocompatibility complex (MHC).

In one example, provided is the transduced T cell as described herein, wherein the cell comprises a second antigen binding receptor capable of specific binding to an antigen selected from the group consisting of FAP, CEA, p95, BCMA, EpCAM, MSLN, MCSP, HER-1, HER-2, HER-3, CD19, CD20, CD22, CD33, CD38, CD52Flt3, FOLR1, Trop-2, CA-12-5, HLA-DR, MUC-1 (mucin), A33-antigen, PSMA, PSCA, transferrin-receptor, TNC (tenascin), CA-IX and PDL1, or to a peptide bound to a molecule of the human major histocompatibility complex (MHC).

In one example, provided is the transduced T cell as described herein, wherein the cell comprises a first antigen binding receptor capable of specific binding to a first tumor associated antigen (TAA), and wherein the cell comprises a second antigen binding receptor capable of specific binding to a TAA.

In one example, provided is the transduced T cell as described herein, wherein the cell comprises a first antigen binding receptor capable of specific binding to programmed death-ligand 1 (PDL1), and wherein the cell comprises a second antigen binding receptor capable of specific binding to an antigen selected from the group consisting of fibroblast activation protein (FAP), carcinoembryonic antigen (CEA), mesothelin (MSLN), CD20, folate receptor 1 (FOLR1), and tenascin (TNC).

In one example, provided is the transduced T cell as described herein, wherein the cell comprises a first antigen binding receptor capable of specific binding to PDL1, and wherein the cell comprises a second antigen binding receptor capable of specific binding to CD20.

In one example, provided is the transduced T cell as described herein, wherein the transduced T cell is co-transduced with a T cell receptor (TCR) capable of specific binding of a target antigen.

Provided is the antigen binding receptor as described herein or the transduced T cell as described herein for use as a medicament.

In another aspect, provided is the transduced T cell as described herein for use as a medicament.

Provided is the antigen binding receptor as described herein or the transduced T cell as described herein for use in the treatment of a malignant disease, wherein the treatment comprises administration of a transduced T cell expressing the antigen binding receptor.

In another aspect, provided is the transduced T cell as described herein for use in the treatment of a malignant disease, wherein the treatment comprises administration of a transduced T cell expressing the antigen binding receptor.

In one example, provided is the antigen binding receptor or the transduced T cell for use as described herein, wherein said malignant disease is selected from cancer of epithelial, endothelial or mesothelial origin and cancer of the blood.

In one example, provided is the transduced T cell for use as described herein, wherein the transduced T cell is derived from a cell isolated from the subject to be treated.

In one example, provided is the transduced T cell for use as described herein, wherein the transduced T cell is not derived from a cell isolated from the subject to be treated.

Provided is a method of treating a disease in a subject, comprising administering to the subject a transduced T cell capable of expressing the antigen binding receptor as described herein. In one example, the method additionally comprises isolating a T cell from the subject and generating the transduced T cell by transducing the isolated T cell with the polynucleotide as described herein, the composition as described herein or the vector as described herein. In one example, the T cell is transduced with a retroviral or lentiviral vector construct or with a non-viral vector construct. In one example, the non-viral vector construct is a sleeping beauty minicircle vector. In one example, the transduced T cell is administered to the subject by intravenous infusion. In one example, the transduced T cell is contacted with anti-CD3 and/or anti-CD28 antibodies prior to administration to the subject. In one example, the transduced T cell is contacted with at least one cytokine prior to administration to the subject, preferably with interleukin-2 (IL-2), interleukin-7 (IL-7), interleukin-15 (IL-15), and/or interleukin-21, or variants thereof. In one example, the disease is a malignant disease. In one example, the disease is selected from cancer of epithelial, endothelial or mesothelial origin and cancer of the blood.

In another aspect, provided is a method for inducing lysis of a target cell, comprising contacting the target cell with a transduced T cell capable of expressing the antigen binding receptor as described herein. In one example, the target cell is a cancer cell. In one example, the target cell expresses an antigen selected from the group consisting of FAP, CEA, p95, BCMA, EpCAM, MSLN, MCSP, HER-1, HER-2, HER-3, CD19, CD20, CD22, CD33, CD38, CD52Flt3, FOLR1, Trop-2, CA-12-5, HLA-DR, MUC-1 (mucin), A33-antigen, PSMA, PSCA, transferrin-receptor, TNC (tenascin), CA-IX and PDL1. In one example, the target cell expresses an antigen selected from the group consisting of fibroblast activation protein (FAP), carcinoembryonic antigen (CEA), mesothelin (MSLN), CD20, folate receptor 1 (FOLR1), tenascin (TNC), and programmed death-ligand 1 (PDL1).

Provided is the use of the antigen binding receptor as described herein, the polynucleotide as described herein, the composition as described herein, or the transduced T cell as described herein for the manufacture of a medicament. In one example, the medicament is for treatment of a malignant disease. In one example, the malignant disease is selected from cancer of epithelial, endothelial or mesothelial origin and cancer of the blood.

In another aspect, provided is the use of the transduced T cell as described herein in the manufacture of a medicament for the treatment of a malignant disease.

CLAIMS

1. An antigen binding receptor comprising an anchoring transmembrane domain and an extracellular domain comprising an antigen binding moiety, wherein the antigen binding moiety is a Fab or crossFab, wherein the antigen binding receptor comprises, at least one stimulatory signaling domain and at least one co-stimulatory signaling domain, wherein the at least one stimulatory signaling domain is the intracellular domain of CD3z, wherein the at least one co-stimulatory signaling domain is the CD28 intracellular domain.

2. The antigen binding receptor of claims 1, wherein the anchoring transmembrane domain is a transmembrane domain selected from the group consisting of the CD8, the CD3z, the FCGR3A, the NKG2D, the CD27, the CD28, the CD137, the OX40, the ICOS, the DAP10 or the DAP12 transmembrane domain.

3. The antigen binding receptor of any one of claims 1 or 2, wherein the anchoring transmembrane domain is the CD28 transmembrane domain, in particular wherein the anchoring transmembrane domain comprises the amino acid sequence of SEQ ID NO:14.

4. The antigen binding receptor of any one of claims 1 to 3, wherein the at least one stimulatory signaling domain comprises the amino acid sequence of SEQ ID NO:16.

5. The antigen binding receptor of any one of claims 1 to 4, wherein the at least one co-stimulatory signaling domain comprises the amino acid sequence of SEQ ID NO:15.

6. The antigen binding receptor of any one of claims 1 to 5, wherein the antigen binding moiety comprises a heavy chain constant domain (CH) and a light chain constant domain (CL), wherein the CH domain or the CL domain is connected at the C-terminus to the N-terminus of the anchoring transmembrane domain, optionally through a peptide linker.

7. The antigen binding receptor of any one of claims 1 to 6, wherein the antigen binding receptor comprises one co-signaling domain, wherein the co-signaling domain is connected at the N-terminus to the C-terminus of the anchoring transmembrane domain.

8. The antigen binding receptor of claim 7, wherein the antigen binding receptor additionally comprises one stimulatory signaling domain, wherein the stimulatory signaling domain is connected at the N-terminus to the C-terminus of the co-stimulatory signaling domain.

9. The antigen binding receptor of any one of claims 1 to 8, wherein the antigen binding moiety is capable of specific binding to an antigen selected from the group consisting of fibroblast activation protein (FAP), carcinoembryonic antigen (CEA), mesothelin (MSLN), CD20, folate receptor 1 (FOLR1), tenascin (TNC) and programmed death-ligand 1(PDL1).

10. The antigen binding receptor of any one of claims 1 to 9, wherein the at least one antigen binding moiety is a capable of specific binding to CD20, wherein the antigen binding moiety comprises:

(i) a heavy chain variable region (VH) comprising

(a) the heavy chain complementarity-determining region (CDR H) 1 amino acid sequence YSWIN (SEQ ID NO:1);

(b) the CDR H2 amino acid sequence RIFPGDGDTDYNGKFKG (SEQ ID NO:2); and

(c) the CDR H3 amino acid sequence NVFDGYWLVY (SEQ ID NO:3); and

(ii) a light chain variable region (VL) comprising

(d) the light chain complementary-determining region (CDR L) 1 amino acid sequence RSSKSLLHSNGITYLY (SEQ ID NO:4);

(e) the CDR L2 amino acid sequence QMSNLVS (SEQ ID NO:5); and

(f) the CDR L3 amino acid sequence AQNLELPYT (SEQ ID NO:6).

11. The antigen binding receptor of any one of claims 1 to 9, wherein the antigen binding moiety is a capable of specific binding to PDL1, wherein the antigen binding moiety comprises:

(i) a heavy chain variable region (VH) comprising

(a) the heavy chain complementarity-determining region (CDR H) 1 amino acid sequence DSWIH (SEQ ID NO:68);

(b) the CDR H2 amino acid sequence WISPYGGSTYYADSVKG (SEQ ID NO:69); and

(c) the CDR H3 amino acid sequence RHWPGGFDY (SEQ ID NO:70); and

(ii) a light chain variable region (VL) comprising

(d) the light chain complementary-determining region (CDR L) 1 amino acid sequence RASQDVSTAVA (SEQ ID NO:71);

(e) the CDR L2 amino acid sequence SASFLYS (SEQ ID NO:72); and

(f) the CDR L3 amino acid sequence QQYLYHPAT (SEQ ID NO:73).

12. The antigen binding receptor of any one of claims 1 to 9, wherein the antigen binding moiety is a capable of specific binding to CEA, wherein the antigen binding moiety comprises:

(i) a heavy chain variable region (VH) comprising

(a) the heavy chain complementarity-determining region (CDR H) 1 amino acid sequence EFGMN (SEQ ID NO:138);

(b) the CDR H2 amino acid sequence WINTKTGEATYVEEFKG (SEQ ID NO:139); and

(c) the CDR H3 amino acid sequence WDFAYYVEAMDY (SEQ ID NO:140); and

(ii) a light chain variable region (VL) comprising

(d) the light chain complementary-determining region (CDR L) 1 amino acid sequence KASAAVGTYVA (SEQ ID NO:141);

(e) the CDR L2 amino acid sequence SASYRKR (SEQ ID NO:142); and

(f) the CDR L3 amino acid sequence HQYYTYPLFT (SEQ ID NO:143).

13. The antigen binding receptor of any one of claims 1 to 9, wherein the antigen binding moiety is a capable of specific binding to CEA, wherein the antigen binding moiety comprises:

(i) a heavy chain variable region (VH) comprising

(a) the heavy chain complementarity-determining region (CDR H) 1 amino acid sequence DTYMH (SEQ ID NO:148);

(b) the CDR H2 amino acid sequence RIDPANGNSKYVPKFQG (SEQ ID NO:149); and

(c) the CDR H3 amino acid sequence FGYYVSDYAMAY (SEQ ID NO:150); and

(ii) a light chain variable region (VL) comprising

(d) the light chain complementary-determining region (CDR L) 1 amino acid sequence RAGESVDIFGVGFLH (SEQ ID NO:151);

(e) the CDR L2 amino acid sequence RASNRAT (SEQ ID NO:152); and

(f) the CDR L3 amino acid sequence QQTNEDPYT (SEQ ID NO:153).

14. An isolated polynucleotide encoding the antigen binding receptor of any one of claims 1 to 13.

15. A vector comprising the isolated polynucleotide of claim 14.

16. The vector of claim 15, wherein the vector is an expression vector.

17. A transduced T cell capable of expressing at least one of the antigen binding receptor of any one of claims 1 to 13.

18. The transduced T cell of claim 17, wherein the cell comprises a first antigen binding receptor according to any one of claims 1 to 13, wherein a first antigen binding receptor comprises a Fab antigen binding moiety, and wherein the cell comprises a second antigen binding receptor according to any one of claims 1 to 13, wherein the second antigen binding receptor comprises a crossFab antigen binding moiety.

19. The transduced T cell of any one of claims 17 or 18 for use as a medicament.

20. The transduced T cell of any one of claims 17 to 18 for use in the treatment of a malignant disease, wherein the treatment comprises administration of a transduced T cell expressing the antigen binding receptor.

21. The transduced T cell for use according to claim 20, wherein said malignant disease is selected from cancer of epithelial, endothelial or mesothelial origin and cancer of the blood.

22. A method for inducing lysis of a target cell, comprising contacting the target cell with a transduced T cell capable of expressing the antigen binding receptor of any one of claims 1 to 13.

23. Use of the transduced T cell of any one of claims 17 or 18 in the manufacture of a medicament for the treatment of a malignant disease.

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